

AMENDMENTS TO THE SPECIFICATION

Please amend the specification to enter the revised Sequence Listing submitted concurrently herewith.

Please replace the paragraph beginning at line 26 of page 3 and extending through line 4 of page 4, with the following amended paragraph:

-- The following sequences of the human DPPIV amino acid sequence are important for the catalytic activity of DPPIV: (i) Tyr⁶²⁷GlyTrpSerTyrGlyGlyTyrVal (SEQ ID NO: 9); (ii) Ala⁷⁰⁷AspAspAsnValHisPhe (SEQ ID NO: 10); (iii) Glu⁷³⁸AspHisGlyIleAlaGln (SEQ ID NO: 11); and (iv) Tyr²⁰¹ValTyrGluGluGluVal (SEQ ID NO: 12) [25-28]. As described herein, the alignment of the following sequences of DPP8: His⁷³⁶GlyTrpSerTyrGlyGlyTyrLeu (SEQ ID NO: 13); Leu⁸¹⁶AspGluAsnValHisPheAla (SEQ ID NO: 14); Glu⁸⁴⁷ArgHisSerIleArg (SEQ ID NO: 15) and Phe²⁵⁵ValLeuGlnGluGluPhe (SEQ ID NO: 16) with sequences (i) to (iv) above, respectively, suggests that these sequences of DPP8 are likely to confer the catalytic activity of DPP8. Thus, in a second aspect, the invention provides a peptide comprising the following amino acid sequences: His⁷³⁶GlyTrpSerTyrGlyGlyTyrLeu (SEQ ID NO: 13); Leu⁸¹⁶AspGluAsnValHisPheAlaHis (SEQ ID NO: 17); Glu⁸⁴⁷ArgHisSerIleArg (SEQ ID NO: 15) and Phe²⁵⁵ValLeuGlnGluGluPhe (SEQ ID NO: 16); which has the substrate specificity of the sequence shown in SEQ ID NO:1. --

Please replace the paragraph at lines 6-25 of page 4, with the following amended paragraph.

-- Also described herein, using multiple sequence alignment, it is observed that DPP8 has 55% amino acid similarity and 32% amino acid identity with a *C. elegans* protein. Further, as shown herein, a nucleic acid molecule which encodes DPP8, is capable of hybridising specifically with DPP8 sequences derived from non-human species. Together these data

suggest that DPP8 is expressed in non-human species. Thus in a third aspect, the invention provides a peptide which has at least 60% amino acid identity with the amino acid sequence shown in SEQ ID NO:1, and which has the substrate specificity of the sequence shown in SEQ ID NO:1. Preferably, the amino acid identity is 75%. More preferably, the amino acid identity is 95%. Amino acid identity is calculated using GAP software [GCG Version 8, Genetics Computer Group, Madison, WI, USA] as described further herein. Typically, the non-human DPP8 comprises the following sequences:

His⁷³⁶GlyTrpSerTyrGlyGlyTyrLeu (SEQ ID NO: 13); Leu⁸¹⁶AspGluAsnValHisPheAlaHis (SEQ ID NO: 17); Glu⁸⁴⁷ArgHisSerIleArg (SEQ ID NO: 15) and Phe²⁵⁵ValLeuGlnGluGluPhe (SEQ ID NO: 16). --

Please replace the paragraph beginning at line 27 of page 4 and continuing through line 23 of page 5, with the following amended paragraph:

-- In view of the homology between DPPIV and DPP8 amino acid sequences, it is expected that these sequences will have similar tertiary structure. This means that the tertiary structure of DPP8 is likely to include the seven-blade β -propeller domain and the α/β hydrolase domain of DPPIV. These structures in DPP8 are likely to be conferred by the regions comprising β -propeller, Gly¹⁸⁰ to Asp⁶⁰⁶, α/β hydrolase, Ser⁶⁰⁷ to Ile⁸⁸² and about 70 to 100 residues in the region Arg³⁹ to Gln¹⁷⁹. As it is known that the β -propeller domain regulates proteolysis mediated by the catalytic triad in the α/β hydrolase domain of prolyl oligopeptidase, [29] it is expected that truncated forms of DPP8 can be produced, which have the substrate specificity of the sequence shown in SEQ ID NO:1, comprising the regions referred to above (His⁷³⁶GlyTrpSerTyrGlyGlyTyrLeu (SEQ ID NO: 13); Leu⁸¹⁶AspGluAsnValHisPheAlaHis (SEQ ID NO: 17); Glu⁸⁴⁷ArgHisSerIleArg (SEQ ID NO: 15) and Phe²⁵⁵ValLeuGlnGluGluPhe (SEQ ID NO: 16)) which confer the catalytic specificity of DPP8. Examples of truncated forms of DPP8 which might be prepared are those in which the region conferring the β -propeller domain and the α/β hydrolase domain are spliced

together. Other examples of truncated forms include those which are encoded by splice variants of DPP8 mRNA. Thus although, as described herein, the biochemical characterisation of DPP8 shows that DPP8 consists of 882 amino acids and has a molecular weight of about 100kDa, it is recognised that truncated forms of DPP8 which have the substrate specificity of the sequence shown in SEQ ID NO:1, may be prepared using standard techniques [30,31]. Thus in a fourth aspect, the invention provides a fragment of the sequence shown in SEQ ID NO: 1, which has the substrate specificity of the sequence shown in SEQ ID NO:1. Preferably, the fragment has an amino acid sequence shown in SEQ ID NO: 3, 5 or 7. --

Please replace the paragraph beginning at line 31 of page 23 and continuing through line 53 of page 24, with the following amended paragraph:

-- RNA (1µg) was reverse-transcribed using the Superscript II enzyme kit (Gibco-BRL) as described previously [42]. PCR using DPP8-pr18 (CTGTGACGCCACTAATTATCTATG; SEQ ID NO: 18) as the forward primer and DPP8-pr26R (CCTAGAGAGGCTAGGGTATTCAAG; SEQ ID NO: 198) as the reverse primer was used to detect full-length DPP8 mRNA. The glyceraldehyde-3-phosphate dehydrogenase (G3PDH) control primer set was G3PDH for (ACCACAGTCCATGCCATCAC; SEQ ID NO: 20) and G3PDHrev (TCCACCACCCTGTTGCTGTA; SEQ ID NO: 21) to give a 470-bp product. --

Please replace the paragraph beginning at line 29 of page 24 and continuing through line 7 of page 25, with the following amended paragraph:

-- The two peptides used were:

PEPTIDE Name: TEDDA-N

SEQUENCE: CTGYTERYMGHPDQNEQG-NH₂ (SEQ ID NO: 22).

This is amino acids 773 to 789, plus a Cys at the N-terminus.

PEPTIDE Name: TEDDR-C

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SEQUENCE: GKPYDLQIYPQERHSC-NH2 (SEQ ID NO: 23).

This is amino acids 836 to 850, plus a Cys at the C-terminus. --

Please cancel the original Abstract and replace it with the new Abstract presented on the following page: